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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/835,976	04/16/2001	David B. Mount	1242/26/2	3961

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EXAMINER	
WEGERT, SANDRA L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 01/24/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/835,976	MOUNT ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *9/26/06*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-11 and 13-104* is/are pending in the application.

4a) Of the above claim(s) *1-6,8-10,14-58,60-100 and 104* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *7,11,13,59 and 101-103* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *16 April 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

A request for continued examination (RCE) under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. This application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid.

Status of Application, Amendments, and/or Claims

The amendment and "Remarks," submitted 26 September 2005 have been entered into the record. Claim 12 is cancelled. Claim 104 is new. It should be noted that claims will be examined insofar as they read on the elected Invention. Claims 1-6, 8-10, 14-58 and 60-100 and 104 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected Inventions, there being no allowable generic or linking claim.

Claims 7, 11, 13, 59 and 101-103 are under examination in the Instant Application.

Maintained/New Objections and/or Rejections

Claim Rejections - 35 USC § 112, first paragraph – scope of enablement.

Claims 7, 11, 13, 59 and 101-103 are rejected under 35 USC 112, first paragraph, because the specification, while being enabling for the polynucleotide of SEQ ID NO: 15, encoding a KCC3 Potassium-chloride cotransporter, does not enable a polypeptide encoded by a nucleic acid sequence having 90% or more sequence identity to the nucleotide of SEQ ID NO: 15. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with the claims.

The specification does not reasonably provide enablement for use of variants of SEQ ID NO: 15 as recited in claims 7, 11, 13, 59 and 101-103. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims. The claims recite a nucleic acid having 90% sequence identity to the KCC3 nucleotide of SEQ ID NO: 15. The claims also embrace variants of the SEQ ID NO: 16, such as a peptide that has *potassium-chloride cotransporter activity*, or those that are immunologically cross-reactive, or those encoded by a nucleic acid that hybridizes to the first 434 nucleotides of SEQ ID NO: 15.

The instant Application does not reasonably provide enablement for various protein forms of the KCC3 transporter, wherein the nucleic acid sequence is 90% identical to SEQ ID NO: 15, with the assurance that enabled proteins that are functionally equivalent to SEQ ID NO: 16 can be made without undue experimentation and with the assurance that they would have the desired properties of the claimed KCC3A transporter. There are no examples of what specific polynucleotides fall within the range of those that would be 90% identical. Furthermore, the claims embrace numerous polypeptides not encompassed by the specification, including those proteins that are structurally dissimilar but serve the same functions within a cell or organism. The specification does not disclose how to use all such variants.

Applicants argue that because the transporters are all transcribed from similar exons (see Figures 1 and 2, instant Specification) at the same gene loci in mouse versus humans, and because of their high homologies, that all claimed transporters should be considered one invention (Remarks, 26 September 2005, page 17).

Applicant's arguments, filed 26 September 2005, have been fully considered but they are not persuasive for the following reasons:

The breadth of claims 7, 11, 13, 59 and 101-103 is too large since the specification fails to provide any guidance on how to produce a nucleic acid which is at least 90% identical to SEQ ID NO: 15 and retains the function of SEQ ID NO: 15. Claims 7, 11, 13, 59 and 101-103 refer to any polynucleotide or polypeptide, that is "at least 90% identical" to that of SEQ ID NO: 15 or 16, without knowledge of the polynucleotides or polypeptides that would fall within this range. In other words, no discussion or working examples, in the instant case, as to what residues are necessary to maintain the functional characteristics of the claimed polynucleotide are disclosed. The Specification makes clear that the selectivity, sensitivity and activity of the KCC transporters are unique for each protein listed (see Figure 8, for example). As further evidence that the KCC transporters are separate inventions, antibodies made against KCC3 demonstrate a lack of cross-reactivity when tested against other KCC transporters (Figure 27D).

Applicants discuss gene loci and exon splicing for each transporter (page 17, Remarks). However, evolutionarily new receptors and transporters are often made this way, by gene rearrangement. There's nothing unusual in the exons from different transporters within a family bearing a superficial resemblance to one another (Figures 1 and 2). However, one cannot infer that they are functionally equivalent because of that resemblance. Furthermore, the Applicants have shown that the disclosed transporters are indeed functionally different (Figure 8).

The instant claims suggest altering as much as 10% of the polypeptide disclosed in SEQ ID NO: 16. Although transporter family members share several common structural features, relevant art shows that members of a class having high homology do not always share a specific

and substantial functional attribute or utility, despite having structural features in common. Point mutations, for example, serve to illustrate this fact, since a single amino acid mutation can change the substrate specificity of a transporter or inactivate it (Oelmann, S., et al, 2001., J. Biol. Chem. 28(13): 26291). Bisson, *et al* (1993, Crit Rev Biochem Mol Biol, 28:259) studied yeast transporter knockout phenotypes, and found little correlation between homology and the substrate transported. For example, they found that yeast transporters *Gal2* and *Hxt4* displayed 83.7% homology, but *Gal2* appears to transport Galactose, while *Hxt4* appears to transport Glucose (based on knockout phenotype- compare Table 1 and Table 2A). Similarly, Liang et al found that only a few amino acid substitutions in glucose transporters can change substrate specificity dramatically (1998, Liang, H., et al, Mol. Cell. Biol. 18(2): 926). These examples and others illustrate that it is not predictable as to which amino acids are necessary to maintain the functional characteristics of a protein.

In summary, the specification does not provide a description of a repeatable process of producing, nor of working examples of making the polypeptides whose amino acid sequences deviate from the disclosed sequence (SEQ ID NO: 16) by as much as 10%. In addition, the predictability of the art is low with regards to the knowledge of what effects altering as much as 10% of the sequence of a polypeptide would have on the polypeptide. For this reason, undue experimentation would be required to determine a structure-function relationship for each possible polypeptide encompassed by the claims.

Conclusion: Claims 7, 11, 13, 59 and 101-103 are rejected for the reasons recited above.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW

19 January 2006

Brenda Brumback

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